

## **POLYURIA AND POLYDIPSIA (PU/PD) IN HORSES**

### **Definition of Polyuria (PU) and polydipsia (PD)**

PD in adult horses can be defined as **water consumption >100 ml/kg daily (>10% BWT)** although lesser intakes might sometimes be judged excessive depending on the managerial/dietary/physiologic conditions.

Typical normal water intake for horses is between 40 and 60 ml/kg daily (4-6% BWT) although could be as low as 10-15 ml/kg daily (1-1½% BWT) in grazing horses or as high as 80-90 ml/kg daily (8-9% BWT) in lactating mares, horses in hard work and in hot environmental conditions. Smaller breeds tend to drink relatively more per kg BWT than larger breeds due to the effects of metabolic body size.

PU is usually defined as **urine production > 50 ml/kg daily (5% BWT)**. Normal urine production is typically between 15 and 30 ml/kg daily (1½ - 3% BWT) and faeces represent the major route of water loss in normal horses.

### **Normal, physiologic causes of PU and/or PD**

<b>PD ONLY</b>	<ul style="list-style-type: none"> <li>- <i>lactation</i></li> <li>- <i>hot weather</i></li> <li>- <i>heavy work</i></li> <li>- <i>diarrhoea</i></li> </ul>
<b>PU&amp;PD</b>	<ul style="list-style-type: none"> <li>- <i>excessive dietary protein (eg &gt;10-12%)</i></li> <li>- <i>excessive salt consumption</i></li> <li>- <i>glucocorticoid and diuretic administration</i></li> </ul>

### **Disease-related, pathophysiologic causes of PU and PD**

<b>COMMON</b>	<ul style="list-style-type: none"> <li>- <i>Primary (psychogenic) polydipsia</i></li> <li>- <i>Cushing's disease</i></li> </ul>
<b>UNCOMMON</b>	<ul style="list-style-type: none"> <li>- <i>Chronic renal failure</i></li> <li>- <i>Hepatic insufficiency</i></li> <li>- <i>Diabetes mellitus (types 1 or 2)</i></li> <li>- <i>Diabetes insipidus</i></li> </ul>

## **INVESTIGATION OF PU/PD**

The limited list of common differential diagnoses makes PU/PD an attractive problem to investigate in horses if a logical approach is followed.

### **1. Quantify and confirm the presence of PD (and PU?)**

Pathophysiologic causes will invariably lead to both PU and PD even though only one and not the other may be recognised and reported by the owner. Therefore it is both easier and diagnostically acceptable to verify and quantify water intake only. Quantification of urine production can be achieved but is less practical. Quantification of water intake should always be performed over a full 24 hour period at least as there are often intraday periodic bursts of drinking associated with post-feeding dehydration for example. It is usual to quantify water intake in horses during a 24 hour period of being fully stabled.

- If water intake is >100 ml/kg/day (>10% BWT) then PD is confirmed and PU is almost inevitable.
- If water intake is <70 ml/kg/day (<7% BWT) then PD is not confirmed. In such cases it may be that the horse is normal and the owner has been misled (eg by short term PD during a few hours but overall normal 24 hour water intake) or alternatively that the horse drank less than usual during the quantification period (eg due to a managemental change/disturbance due the usual procedure of 24 hour stabling for water intake quantification). If the owner's report of PD is convincing then attempts to quantify water intake under normal management circumstances should be performed.
- If water intake is 70-100 ml/kg/day (7-10% BWT) then PD may be suspected if there are no apparent physiologic causes (see above).

### **2. Initial (simple) blood and urine tests**

#### **Haematology**

- i. **Anaemia** is a common finding with CRF due to effect of uraemia and reduced erythropoietin synthesis. Polycythaemia may arise through dehydration suggesting that PU is the primary problem rather than PD (eg DI).
- ii. **Neutrophilia** is a common response to endogenous (ie PPID) and exogenous glucocorticoids (usually with lymphopaenia) and may also be an indicator of inflammatory disease.

#### **Serum biochemistry**

- i. Usually **urea** >15 mmol/L and **creatinine** >300 µmol/L are seen in CRF cases. More modest increases (eg urea 8-12 mmol/L, creatinine 180-250 µmol/L) more commonly indicate dehydration but could suggest early/mild CRF. Low urea (< 4 mmol/L) and creatinine (<75 µmol/L) may occur in hepatic insufficiency or in cases of primary (psychogenic) polydipsia with washout.
- ii. Persistent **hyperglycaemia** is sometimes seen in PPID cases. Serum glucose between 7-10 mmol/L may serve as a diagnostic indicator of PPID although hyperglycaemia is unlikely to cause PU/PD until >10 mmol/L (≈renal threshold).
- iii. **Hypercalcaemia** (total Ca > 3.5 mmol/L, ionised Ca > 1.7 mmol/L) is often seen in CRF (Paraneoplastic disease is the main alternative cause of hypercalcaemia).
- iv. **GGT** and **AST** used to rule out liver disease.

## Urinalysis

When catheterised urine samples are obtained, consideration of the effects of sedation is important.  $\alpha_2$  agonist sedatives (detomidine, xylazine, romifidine) have both acute diuretic and hyperglycaemic effects. The diuretic effect is unlikely to alter the properties of the subsequently collected urine sample as a few mLs of most recently produced diuresed urine should not significantly affect the previously accumulated urine in the bladder. However, even a small amount of glycosuria might confuse diagnostic interpretation. Hence acepromazine (5-10 mg/100kg iv) perhaps supplemented by a nose twitch or a small dose of detomidine (0.5 mg/100 kg iv) should be used as necessary in geldings. In mares the use of stocks or a stable door may avoid the need for sedation.

### i. **Specific gravity**

- **SG <1.008 (hyposthenuria)** suggests that the kidney is actively excreting water and is typical of primary (psychogenic) PD and DI.
- **SG between 1.008-1.014 (isosthenuria)** suggests that the kidney is neither actively concentrating nor diluting the filtrate and is consistent with (but not diagnostic for) CRF. Although isosthenuria is typical of CRF, other causes of PU/PD might coincidentally happen to fall in the isosthenuric range. Therefore, when isosthenuric samples are obtained, serum urea and creatinine should be checked to rule in or rule out possible CRF.
- **SG >1.014 (hypersthenuria)** indicates that the kidney is actively concentrating urine although **SG >1.020** is usually regarded as more convincing of good concentrating ability (and therefore absence of CRF).

- ii. **Glycosuria** – if persistent then this indicates diabetes mellitus and usually PPID although primary *diabetes mellitus* is a rare possibility (cross check with serum insulin). (N.B. acute stress or  $\alpha_2$  agonist sedatives also cause hyperglycaemia and glycosuria).
- iii. **Urine creatinine : serum creatinine ratio** is useful in cases with equivocal mild increases in serum creatinine concentration (eg 180-250  $\mu\text{mol/L}$ ). Mild to moderate increases in serum creatinine due to dehydration will be expected to be matched by high urine creatinine concentrations (>50 x serum concentration) whereas CRF cases will have lower urine creatinine (eg <40 x serum creatinine).
- iv. **Enzymuria** – urinary GGT, AP and LDH may all be raised in CRF due to tubular damage (more so in acute renal failure). Urinary GGT is the most commonly assayed urinary enzyme and is usually similar in concentration to serum levels (ie <40 iu/L urine). Clearly adjustments should be made for urine concentration and this is done by comparison with urine creatinine concentration (expressed in mmol/L, not  $\mu\text{mol/L}$ ):

$$\frac{\text{urinary GGT (iu/L)}}{\text{urinary creatinine (mmol/L)}} < 5.0 \text{ iu/mmol}$$

### **3. Further laboratory tests**

On the basis of the above results it should be possible to confirm/rule out many differential diagnoses including CRF, *diabetes mellitus* and liver disease.

PPID (if not already suspected from hyperglycaemia and glycosuria) is usually suggested by typical clinical signs (old, hairy, laminitic etc.), overnight dexamethasone suppression test or resting ACTH concentration (see separate notes on endocrinopathies).

The most useful tests to use to differentiate primary (psychogenic) polydipsia from *diabetes insipidus* are ***the water deprivation test, modified water deprivation test, serum ADH concentration*** and, possibly, the ***ADH response test***.

#### **a. The Water Deprivation Test**

The purpose of this test is used to help differentiate primary (psychogenic) polydipsia from diabetes insipidus in subjects found to be producing hyposthenuric urine (urine SG < 1.008). This test must not be performed on azotaemic horses suspected to have renal compromise. The object of the test is to establish whether or not the horse can produce concentrated urine (psychogenic polydipsia cases can; diabetes insipidus cases cannot).

#### Technique

- Weigh horse accurately (*if possible*)
- Check serum urea and creatinine are normal (*if not don't proceed*)
- Take baseline urine sample and measure SG (*will usually be < 1.008 in cases requiring this test*)
- Keep horse stabled and remove water
- Check serum urea and creatinine and urinary SG at least every 6 hours (*and reweigh if possible*)

The end of test is when one of the following occurs:

- 24 hours water deprivation
- 5% reduction in bodyweight
- clinical signs of dehydration
- azotaemia develops
- urinary SG > 1.020

#### Interpretation

- if SG rises above 1.020 this confirms renal concentrating ability is present and therefore psychogenic polydipsia
- if urine SG stays < 1.020 and horse becomes dehydrated or loses 5% bodyweight this suggests *diabetes insipidus* (often happens by 12 hours with DI), although could be psychogenic polydipsia associated with 'medullary washout'
- if urine SG is still low after 24 hours but horse shows no clinical signs of marked dehydration this implies psychogenic polydipsia associated with 'medullary washout', although could be *diabetes insipidus*

**b. The Modified Water Deprivation Test**

This test is used to differentiate equivocal cases of diabetes insipidus from psychogenic polydipsia as described above. However, most DI cases will become rapidly dehydrated within 12 hours of initial water deprivation and therefore this test is really used to confirm the suspected diagnosis of psychogenic polydipsia with medullary washout that has prevented urinary concentration within 24 hours of water deprivation in the standard initial water deprivation test. However, the test can justifiably be used instead of the initial water deprivation test as it may be easier and possibly safer to perform.

Perform instead of a standard water deprivation test or start immediately following standard water deprivation test (above) if:

- urine SG < 1.020 after 24 hours water deprivation
- < 5% reduction in bodyweight
- no azotaemia
- no clinical signs of dehydration

Technique

- Allow water consumption equivalent to 40 ml/kg BWT daily (4% BWT) offered in several aliquots through the day to avoid immediate consumption of the total daily ration
- Continue for up to 2-3 days or until one of the criteria above is reached
- Measure serum BUN and creatinine and urinary SG at least every 6 hours

Interpretation

- If urine SG rises above 1.020 this confirms primary (psychogenic) polydipsia.
- Progressive dehydration and continued inability to concentrate urine implies *diabetes insipidus*.

**c. Serum ADH (vasopressin) concentrations**

In normal hydrated horses this is reported to be typically between 1 - 2 pg/mL. In response to 24 h water deprivation a modest increase to typically between 4 - 8 pg/mL is expected but can be much higher (eg 20+). Low resting ADH concentrations and failure of an increase in response to water deprivation imply central *diabetes insipidus*. Both primary (psychogenic) polydipsia and nephrogenic *diabetes insipidus* cases would be expected to have normal ADH concentration and response.

**d. The ADH (vasopressin) response test**

This test is indicated when *diabetes insipidus* is suspected and used to differentiate central from renal (nephrogenic) forms. Central *diabetes insipidus* cases will successfully concentrate urine following exogenous ADH administration whereas nephrogenic *diabetes insipidus* cases shown little to no response to ADH administration ("Pitressin" 20 iu/mL Argipressin; Goldshield Pharmaceuticals).

e. **Urinary fractional electrolyte excretion rates (“Creatinine clearance ratios”)**

This is occasionally useful to perform on simultaneously collected serum and urine samples. It is vital that serum is separated from the cellular fraction promptly as leakage of potassium and phosphate from dying cells will significantly alter serum electrolyte concentrations. For this test it is assumed (slightly incorrectly!) that the sole route of serum creatinine loss is the urine and that it is neither secreted nor absorbed by the kidney. Thus each electrolyte is compared with a substance (creatinine) that is nominally neither secreted nor absorbed to give an impression of the renal handling of each electrolyte.

The clearance (CL) of a substance, “E”, from the plasma is related to its serum (S) and urine (U) concentration, thus:

$$CL_A \times S_A = \text{urine output} \times U_A$$

or:

$$CL_A = \frac{\text{urine output} \times U_A}{S_A}$$

Hence the clearance of any substance (eg an electrolyte, “E”) can be compared to creatinine as a fractional excretion rate (or creatinine clearance ratio) thus:

$$\begin{aligned} \text{Fractional electrolyte excretion rate} &= \frac{\text{urine output} \times U_E}{S_E} \div \frac{\text{urine output} \times U_{CR}}{S_{CR}} \\ &= \frac{U_E \times S_{CR}}{U_{CR} \times S_E} \end{aligned}$$

A value of 1 (or 100%) suggests similar handling to creatinine – ie neither secreted nor absorbed. Values <1 (or <100%) signify active reabsorption of the electrolyte whereas values >1 (or >100%) signify active excretion. Typical normal values comprise:

Na	0.03 – 0.5%	(ie 99.5 - 99.97% filtered Na is reabsorbed)
K	15 - 70%	(ie 30 - 65% filtered K is reabsorbed)
Cl	0.2 – 1.7%	(ie 99.8 - 98.3% filtered Cl is reabsorbed)
Ca	< 7%	(ie >93% filtered Ca is reabsorbed)
PO <sub>4</sub>	<0.5%	(ie >99.5% filtered PO <sub>4</sub> is reabsorbed)
Mg	< 15%	(ie >85% filtered Mg is reabsorbed)

In the context of PU/PD, high values (signifying decreased reabsorption) are consistent with renal failure (esp Na and Cl) although excessive electrolyte consumption should also be considered.

